

REMARKS

The claims have been amended in order to place the application in better form.

Claims 42-59 have been cancelled without prejudice, and Claims 60-79 have been added. The cancellation of Claims 42-59 without prejudice is not to be construed as an admission by Applicants or Applicants' attorneys that such claims are not patentable, and Applicants reserve the right to prosecute such claims in a continuing application.

Claims 42-59 had stood rejected under 35 U.S.C. 102(e) as being anticipated by Johnstone, et al. This rejection is respectfully traversed.

The present invention is directed to process for producing chondrocytes, as defined broadly in Claim 60, and to a process for inducing chondrogenesis in mesenchymal stem cells, as defined broadly in Claim 70. Such processes are effected by culturing mesenchymal stem cells in a chemically defined serum-free medium in vitro wherein the mesenchymal stem cells are associated in a three-dimensional format. The chemically defined serum-free medium comprises (1) a chemically defined minimum essential medium; (2) ascorbate or an analog thereof; (3) an iron source; (4) insulin or an insulin-like growth factor; (5) at least one chondroinductive agent or factor; and (6) a simple sugar, wherein the simple sugar is present in the medium in an amount of from about 3g/l to about 7g/l.

Applicants have discovered, as shown in the examples, that by culturing mesenchymal stem cells in a chondrogenic medium which includes a simple sugar at a concentration of from about 3g/l to about 7g/l, one obtains improved differentiation of mesenchymal stem cells into chondrocytes, as opposed to media which have a lower

sugar concentration, such as, for example, media which have a glucose concentration which is the standard concentration present in "low glucose DMEM" (1g/l).

Johnstone discloses a chondrogenic medium which includes (1) a chemically defined minimum essential medium; (2) ascorbate or an analogue thereof; (3) an iron source; (4) insulin or an insulin-like growth factor; and (5) at least one chondroinductive agent or factor. Although Johnstone states that a glucose-containing medium such as Dulbecco's Modified Eagles's Medium (DMEM) may be used, Johnstone does not disclose or even remotely suggest to one of ordinary skill in the art that the chondrogenic medium may include a simple sugar in an amount of from about 3 g/l to about 7g/l. In fact, the only specific example of DMEM suggested by Johnstone is Dulbecco's Modified Eagle's Medium-Low Glucose (DMEM-LG), which Johnstone states is well suited to the present invention when supplemented with serum. (See Column 6, lines 38-44.) As indicated at Page 11, line 15 of the applicants' specification, "low glucose DMEM" has a glucose concentration of 1g/l. Thus, Johnstone gives as a preferred embodiment of his invention a medium having a glucose concentration of 1g/l, as opposed to a sugar concentration of 3 g/l to 7 g/l as claimed by Applicants. Therefore, Johnstone teaches away from the present invention, and such teaching away from the invention is indicative of non-anticipation and non-obviousness. (See W.L. Gore & Associates, Inc. v. Garlock, Inc., 220 U.S.P.Q. 303 (C.A.F.C. 1983), at 312; United States v. Adams, 383 U.S. 39 (1966)).

Therefore, Johnstone does not anticipate Applicants' processes as claimed, nor does Johnstone render Applicants' processes as claimed obvious to one of ordinary skill in the art. For the above reasons and others, this application is in condition for

allowance, and it is therefore respectfully requested that the rejection under 35 U.S.C. 102(e) be reconsidered and withdrawn and a favorable action is hereby solicited.

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Raymond J. Lillie".

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